UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,484	02/17/2004	David B. Rozema	Mirus.030.16.04	2135

7590 08/31/2006

Mark K. Johnson
Mirus Corporation
505 S. Rosa Rd.
Madison, WI 53719

EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,484	ROZEMA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (New Matter).

3. Instant claim 1 (and those claims dependent thereon) was amended to recite "a membrane active polyamide-biologically active compound." Although the specification as filed provides support for wherein the polymers of the invention encompass a "polyamine," there is no support either explicit or implicit for the present amendment in the specification or claims as originally filed.

"[T]here is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed, Wertheim, 541 F.2d at 262, 191 USPQ at 96; ***however, with respect to newly added or amended claims, applicant should show support in the original disclosure for the new or amended claims. See MPEP § 714.02 and § 2163.06 ("Applicant should * * * specifically point out the support for any amendments made to the disclosure."); and MPEP § 2163.04."***

In the instant case, Applicants have not provided any reference to the specification or claims, as originally filed, to support the amendment to claim 1 filed 10-24-05.

Response to Arguments

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

5. Claims 1-3, 7-8, and 19-20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Heiliger et al. (US 5,453,461), for the reasons of record.

6. Applicant's arguments filed 10-24-05 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the Heiliger et al. patent does not teach conjugation of a biologically active compound to a polymer via a labile, reversible or cleavable linkage. Moreover, Applicants have provided a declaration under 37 CFR 1.132 in support of their arguments.

7. The Declaration under 37 CFR 1.132 filed 10-24-05 is insufficient to overcome the rejection of claims 1-3, 7-8, and 19-20 based upon Heiliger et al. as set forth in the last Office action because contrary to Applicant's assertions above, and the statements made by Dr. Monahan, the Heiliger et al. reference discloses conjugation of a polymer via a labile, cleavable, or reversible linkage.

See for example, col. 9, lines 60-63 of Heiliger et al.

"[T]he units A and P in the polymers according to the invention are bonded to each other, for example, via an ester, sulphonic ester, amide, sulphonamide, urethane, thiourethane, urea, thiourea, ether, amine or sulphide group."

Applicants have not provided any evidence that the above linkages cannot be selectively cleaved, reversibly linked, or labile under any and all conditions. The Monahan Declaration states that "amide, urea, ester and ether groups" would not be considered labile under physiological conditions. However, it is noted that the instant claims are not limited to wherein the term "labile" is limited to "labile under physiological conditions. Moreover, the Declaration does not address the full scope of the possible linkages encompassed by Heiliger et al. Absent evidence to the contrary, the classes of bonds listed in Heiliger for linking the A and P portions of the disclosed conjugates meet the scope of the term "labile," as recited in the instant claims, in particular the sulphide linkage as described by Heiliger et al.

8. Claims 1-8, 16 and 19-20 remain rejected and claims 9-15 are rejected under 35 U.S.C. 102(e or a) as being anticipated by Pinchuk et al. (US 2002/0107330), for the reasons of record.

9. Applicant's arguments filed 10-24-05 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the there are no explicit or implicit teachings in this reference for attachment of a biologically active compound to a polymer via a labile bond or that the polymer be membrane active. Contrary to Applicant's assertions, Pinchuk et al. discloses the following:

[0198] In several examples given above, the therapeutic agent is provided within a matrix comprising the copolymer of the present invention. The therapeutic agent can also be covalently bonded, hydrogen bonded, or electrostatically bound to the

copolymer. As specific examples, nitric oxide releasing functional groups such as S-nitroso-thiols can be provided in connection with the copolymer, or the copolymer can be provided with charged functional groups to attach therapeutic groups with oppositely charged functionalities.

The above passage of Pinchuk et al. teaches that S-nitroso-thiols can be used to attach therapeutic groups with the copolymers of the invention. Applicants have not provided any evidence that the full scope of linkages discussed by Pinchuk et al., in particular the S-nitroso-thiol linkage, cannot be specifically cleaved under the appropriate conditions.

10. Claims 1, 7-8, 17-18 and 19 remain rejected under 35 USC 102(b) as being anticipated by Anderson et al. (US 5,169,933), for the reasons of record.

11. Applicant's arguments filed 10-24-05 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that this reference does not "provide any explicit or implicit teaching of conjugation of a biologically active compound to a polymer via a labile bond."

Contrary to Applicant's assertions, the following passage from column 21 of Anderson et al. provides explicit evidence that a labile bond (as defined by Applicant's specification see pages 7-8) is used to conjugate the polymers of this invention to a biologically active agent:

The purified translocating peptide is conjugated to a heterobifunctional crosslinking reagent, such as succinimidyl 4-(N-maleimido-methyl)cyclohexane-1-carboxylate (SMCC) through its amino terminus. Briefly, the peptide is dissolved in 0.1 M borate buffer, pH 7–9, and the crosslinker, which is dissolved in buffer with as much DMSO as necessary for solubility, is added in equimolar amounts. The peptide-SMCC mixture is reacted for approximately 30 min at room temperature, and the derivatized product is separated using PD-10 gel filtration. The SMCC-derivatized translocating peptide is then combined at a 5:1 ratio with an A chain cytotoxic agent (such as ricin A chain) that has been prereduced with dithiothreitol (DTT) and separated from B chain by reactive blue 2 {(1-amino-4[[4-[[4-chloro-6-[[3(or 4)-sulfophenyl]amino]-1,3,5-triazin-2-yl]amino]-3-sulfophenyl]amino]-9,10-dihydro-9,10-dioxo-2-anthracenesulfonic acid)}-sepharose chromatography. The reduced ricin A chain reacts with the maleimide group of the SMCC-derivatized peptide, forming a thioether bond; unreacted derivitized peptide is quickly removed by gel filtration.

The translocating peptide-modified ricin A chain is reacted with iminothiolane to generate further thiol groups, which are then used to create a disulfide bond with DTT (50 mM)-treated antibody. The translocating peptide-ricin A chain-antibody CLC is separated from unreacted ricin A chain-translocating peptide by gel filtration on an HPLC TSK 3000 column (BioRad, Richmond, Calif.) using a flow rate of 0.5 ml/min in phosphate-buffered saline (PBS), 0.1 M, pH 7.2.

It is clear that the above passage describes the use of a disulfide bond to link polyamine polymers with a biologically active agent, namely an antibody. Therefore, Applicant's assertions regarding the disclosure of this reference are improper. The grounds for this rejection remain for the reasons of record.

Double Patenting

12. The rejection of claims 9-16 over copending application 10/772,502 is withdrawn in response to Applicant's submission of a Terminal Disclaimer (10/24/05) and the appropriate fee (3-20-06).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-5, 7-15, 17, and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolff et al. (US 20010036926).

15. Claims 1-5, 7-15, 17, and 19-20 of the instant application are taught by Wolff et al., for example:

Wolff et al. in paragraph [0108] disclose the formation of a complex between a polymer and a targeting group, wherein the polymer is attached to the targeting group via a cleavable group. The cleavable groups include disulfide bonds, diols, diazo bonds, ester bonds, sulfone bonds, acetals, ketals, enol ethers, enol esters, enamines and imines, acyl hydrazones, and Schiff bases. In a preferred embodiment, a chemical reaction can be used to attach a signal to a nucleic acid complex. The signal can be a protein, peptide, lipid, etc. (see Paragraph [0109-0110]. A specific example of such a signal includes the influenza virus hemagglutinin subunit HA-2 peptides and other types of amphipathic peptides, see paragraph [0112].

According to Wolff et al. the disulfide linkage can be used to connect the molecules of the invention. The reversibility of disulfide bond formation makes them useful tools for the transient attachment of two molecules. The disulfide groups can been used to attach a bioactive compound and another compound, such that when the disulfide bond is reduced the bioactive compound can be released (see paragraph [0003]).

The nucleic acids of Wolff et al. include DNA and RNA compounds, including for example antisense (see paragraph [0122]).

The polymers of the instant invention include those formed from the polymerization of vinyl (see paragraph [0099]. Moreover, the monomers used for polymerization can also contain chemical moieties that can be modified before or after the polymerization including (but not limited to) amines (primary, secondary, and tertiary), amides, carboxylic acid, ester, hydroxyl, hydrazine, alkyl halide, aldehyde, and ketone. (see

paragraph [0103]). Polyethyleneimine and polylysine were used in specific examples to form complexes with nucleic acid via a disulfide linkage, see examples 4 and 5.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-5, 7-15, 17 and 19-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,087,770. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 1-4, 7-12, 17 and 19-20 are anticipated by the claims of the issued US Patent. Additionally, claims 5 and 13-14 are obvious variants of the issued claims.

The instant claims differ from the issued US claims to the extent that the instant claims are broader in scope that the instant claims, the issued claims represent a

species of the broader claims of the instant application. For example, the instant claims require the covalent attachment of a biologically active compound to a polyamine via a labile covalent bond, however the issued claims are limited to the attachment of a nucleic acid (see issued claim 7), to a compound for delivering a molecule (said nucleic acid) into a mammalian cell, wherein said compound is a peptide (see claims 3-6). In regards to instant claims 5 and 13-14, the disclosure of issued US Patent 7,087,770 see col. 18, lines 33-65) defines the term "nucleic acid" as encompassing antisense, ribozymes, and single, double, triple or quadruple DNA or RNA. Therefore, the scope of instant claims 5 and 13-14 represent an obvious alternative embodiment of issued claim 7, based upon the definition of the term "nucleic acid" as set forth in the disclosure of the issued US Patent.

18. Claims 1-5, 7-15, 17 and 19-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Wolff et al. (US 7,087,770), for the reasons given in the above Double Patenting Rejection.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Epps-Ford, Ph.D.
Primary Examiner
Art Unit 1633

JLE